Treatment of venous malformations by direct injection with ethanol

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Purpose: **Venous malformations (VMs) may be discrete or extensive, and larger lesions may be difficult to remove with surgery. Incompletely removed lesions have a tendency to recur. We report our experience with ethanol ablation of VMs.**

Methods: **All 12 patients (seven women; mean age, 37 years) were evaluated with magnetic resonance imaging before treatment. A total of 19 prior surgical excisions had been performed for seven of the patients. Symptoms were present in all 12 patients and included bleeding, pain, swelling, and limitation of exercise. The VMs were present in the lower extremities of seven patients, in the upper extremities of three patients, and in the flank and buttocks in two patients.**

Results: **The 12 patients have undergone 30 injection procedures, with six patients requiring one, three patients requiring two, two patients requiring three, and one patient having undergone 12 treatments. General anesthesia was used in 11 patients. Blood loss was minimal for all procedures, and 28 of the 30 procedures were technically successful. Skin ulceration was seen in approximately half of the treated VMs, all of which healed with local wound care. Focal VMs were injected in six patients and resolved with a single treatment in five patients. Patients were free of symptoms at a mean follow-up of 10 months. Extensive VMs were injected for discrete, symptomatic areas in five patients. These lesions all regressed and were asymptomatic at a mean follow-up of 23 months in all but one patient. However, these lesions required multiple treatments as additional areas became problematic.**

Conclusions: **Ethanol sclerosis is a well-tolerated, safe, and effective adjunct to the management of VMs. Advantages of ethanol injection include the ability to treat a very localized area without an incision. Conversely, extensive lesions may be palliated as symptoms occur. (J Vasc Surg 1997;26:838-44.)**

Venous malformations (VMs) are a difficult entity to treat because they are often extensive and have a tendency to recur after treatment. These low-flow lesions are either capillary or venous malformations that are present at birth and grow with the patient. Although VMs can be limited to subcutaneous tissues, they often grow among muscles, nerves, and blood vessels, which makes them difficult to delineate from normal tissues radiologically.[1] Operative removal of extensive lesions may be difficult and is often accompanied by a large amount of blood loss.

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Because these lesions are often symptomatic, various radiologic interventions have been used in their treatment. Arterial embolization of the nidus via selective catheterization of the feeding vessels, although effective for high-flow arteriovenous malformations and fistulas,[2-9] usually only decreases the size of VMs and does not obliterate the anomalous channels,[10] and therefore should not be used in the treatment of VMs. In contrast, direct puncture of the lesions with installation of a sclerosing agent has been reported to be effective in treating VMs.[1,3,10,11] Ethanol is an effective sclerosing agent and causes necrosis of vessel walls with sludging of red blood cells and subsequent thrombosis. This leads to the eventual production of intimal fibrosis related to ethanol's protein denaturing and hydroscopic properties.[11,12] We report our experience with direct injection of absolute ethanol into a series of VMs to explore the selection, techniques, complications, and results with this treatment.

METHODS

Patients who were treated at Northwestern Memorial Hospital between the years of 1993 and 1996 were eligible for the study. Patients were treated after appropriate informed consent was obtained. Data were collected from chart review, clinic visits, and telephone conversations. All 12 patients (seven women; mean age, 37 years) were evaluated with magnetic resonance imaging (MRI) before treatment. Venograms and arteriograms were also performed for selected patients, and all arteriovenous malformations and fistulas were specifically excluded from this report. A total of 19 prior surgical excisions had been performed for seven of the patients. Symptoms were present in all 12 patients and included bleeding, pain, swelling, and limitation of exercise. The VMs were present in the lower extremities of seven patients, in the upper extremities of three patients, and in the buttock and flank of two patients. Lesions were focal and circumscribed in seven patients and extensively involved the majority of an extremity in five patients. General anesthesia was used for all but one patient because of the extreme pain that follows ethanol injection. Contrast material was injected directly into the lesion to determine the extent of the VM and to estimate the amount of ethanol required to fill the VM in its dilated state without filling normal venous channels. After defining the cavity size, absolute ethanol was then injected directly and contained within the VM using tourniquet, manual compression, or both for 15 to 20 minutes. Residual ethanol was successfully aspirated from some of the lesions, whereas other VMs contained only thrombosed blood. Contrast material was again injected to confirm the extent of VM thrombosis, and further injections of ethanol were used if a residual cavity was demonstrated by contrast injection. Great care was used in the positioning of the needle inside the lesion to prevent extravasation of ethanol, which can cause extensive tissue necrosis. Steroids were used during and after procedures to reduce inflammation, and selected patients were sent home on a Medrol Dose Pack (Upjohn, Kalamazoo, Mich.). Ketoralac was used for analgesia, and the procedure was usually performed on an outpatient or 23-hour admission basis.

Follow-up was measured from the time of treatment to the last contact with the patient at either repeat imaging studies, office visits, or telephone conversations. In the event of multiple treatments, follow-up was measured from the time of the first injection.

RESULTS

A listing of the individual patients and their treatment is provided in Table I. The 12 patients have undergone 30 injection procedures, with six patients requiring one treatment, three patients requiring two treatments, two patients requiring three treatments, and one patient having undergone 12 treatments. The amount of ethanol injected into the lesions ranged from 0.8 to 40 ml, with a mean of 9 ml per session. The estimated blood loss was minimal for all procedures, and 28 of the 30 procedures were technically successful. One procedure early in this series was aborted because of an inability to place the needle into the lesion without extravasation of contrast material. This 2 × 3 cm lesion was surgically excised with a good result. Another patient underwent two successful treatments but still had residual VM that could not be accessed on the third treatment. Extravasation of ethanol was not observed in the 28 successfully performed procedures. Skin ulceration was produced in approximately half of the treated VMs, all of which healed with local wound care that consisted of outpatient debridement and saline wet to dry dressing changes. All wounds healed without operative debridement or skin grafting, although a majority of patients with ulceration required some local debridement as an outpatient. The wounds followed a typical pattern of erythema and induration after injection of ethanol, with blister formation and skin breakdown occurring in approximately half of the wounds. Wound healing time was dependent on the size of the initial skin necrosis, but most wounds healed within 2 to 3 weeks. Skin necrosis typically occurred in the very superficial VM, and the size of the ulceration depended on the size of the treated VM. Nerve damage, another potential complication of ethanol injection, was not seen in the 28 technically successful procedures. Patients typically experienced pain at the injection site for 1 to 2 weeks.

Focal VMs were treated in a total of seven patients, in whom five lesions resolved with a single treatment. Four of these patients had previously been unsuccessfully treated by a total of 12 surgical excisions. Another patient who had a buttock and gluteal VM required three treatments, which ablated the lesion, and his symptoms resolved. These six patients were free of symptoms at a mean follow-up of 10 months. The seventh patient also had a focal VM, but the treatment failed because of the inability to place the needle into the lesion without extravasation of contrast material, and the procedure was aborted.

Patient number 4 had a VM on the left lateral plantar surface of her foot. The lesion was painful,

Table I. Summary of study patients

Patient age/sex	*VM location*	*Symptoms*	*Prior treatments*	*Number of treatments*	*Results*	*Follow-up (mo)*
1. 38/M	Thigh, localized	Hemorrhage	Vein stripping	1	No recurrence of VM or hemorrhage	8
2. 21/F	Calf, localized	Pain and swelling	None	1	No recurrence of VM, asymptomatic	19
3. 28/F	Arm, localized	Pain and throbbing	2 surgical excisions	1	No recurrence of VM	18
4. 30/F	Foot, localized	Pain, difficulty walking	7 surgical excisions	1	VM ablated, asymptomatic	1
5. 48/F	Popliteal fossa, localized	Pain, swelling, exercise limitation	2 surgical excisions	1	VM ablated, asymptomatic	1
6. 31/M	Buttock and gluteal area, localized	Pain with walking and sitting	1 incisional biopsy	3	No recurrence, asymptomatic	12
7. 47/F	Arm, localized	Pain and weakness	None	Inability to place needle without extravasation	Technical failure, surgically excised	NA
8. 41/F	Flank and paraspinal area, extensive	Pain and swelling	Sclerotherapy, 3 surgical excisions, and 1 embolization of feeding veins with coils	3 with failure to cannulate VM on last treatment	VM decreased in size after 2 treatments, unable to access VM for further therapy, patient still has symptoms	29
9. 33/M	Foot and calf, extensive	Hemorrhage	Vein stripping and sclerotherapy	2	Hemorrhage in 2 separate locations controlled	36
10. 22/M	Arm, shoulder, and chest, extensive	Pain, throbbing, and numbness	1 surgical excision	2	Pain resolved in treated areas	11
11. 81/F	Leg, Klippel-Trenaunay, extensive	Refractory bleeding after placement of hip prosthesis	2 hematoma evacuations with ligation of multiple veins	2	Bleeding resolved after second treatment, prosthesis removed 5 months later because of infection	26
12. 27/M	Both legs, buttock, penis, and scrotum, extensive	Hemorrhage and pain	None	12 (ongoing)	Symptomatic areas resolved	15

and she had difficulties walking because of pain and swelling. She had undergone seven prior attempts at surgical excision of the VM. An arteriogram and a venogram (Fig. 1, *A* and *B*) of her foot were normal-appearing. MRI revealed a mass with the typical signal intensities of a VM between the fourth and fifth metatarsals in the deep plantar space extending into the subcutaneous tissues with no bony involvement (Fig. 1, *C*). The VM was injected with 2 ml of absolute ethanol, and a follow-up MRI 1 month later (Fig. 1, *D*) revealed a marked decrease in the size of the VM with residual soft tissue swelling. The patient's symptoms completely resolved. As this case demonstrates, MRI or direct injection of contrast into the lesions is the preferred imaging method because arteriography and venography may not demonstrate the VM or its true extent.

Extensive VMs, usually involving an entire extremity, were injected for discrete, symptomatic areas in four patients, and these treated areas all regressed and were asymptomatic. A fifth patient, who had an extensive VM of the flank and paraspinal area and had undergone multiple attempts at sclerotherapy, three surgical excisions, and embolization of the venous feeding vessels with coils, underwent two successful ethanol treatments, which decreased the size of her VM but did not totally alleviate her symptoms. A third treatment was attempted, but access by direct injection was unable to be obtained and further ethanol treatments could not be per-

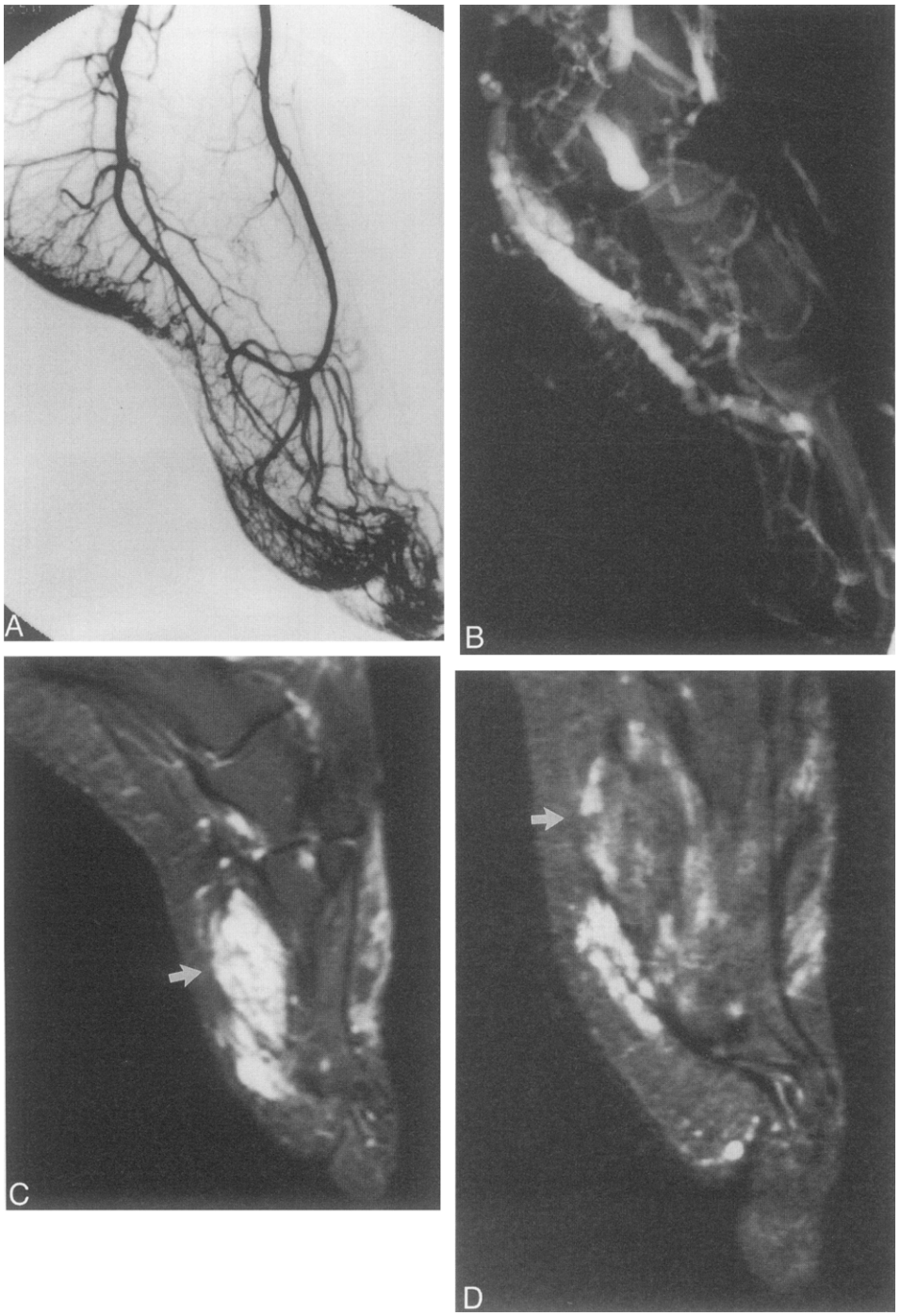

Fig. 1. Various imaging methods in a patient with VM of the left foot. **A,** Normal arteriogram; **B,** normal venogram. **C,** VM between the fourth and fifth metatarsals as a hyperintense (white) signal on this T_2 MRI image *(arrow)*. **D,** T_2 MRI image demonstrates the same area as **C** 1 month after direct injection of ethanol into the lesion *(arrow)*. Notice the greatly decreased size of the VM as well as the residual soft tissue swelling from the procedure.

formed. The five patients had a total of 21 treatments, and the mean follow-up of these patients is 23 months. Ethanol injection was successful in palliating these extensive VMs; however, these lesions may require multiple treatments as additional areas become problematic.

Patients 11 and 12 (see Table I) are of particular interest and demonstrate the versatility of direct eth-

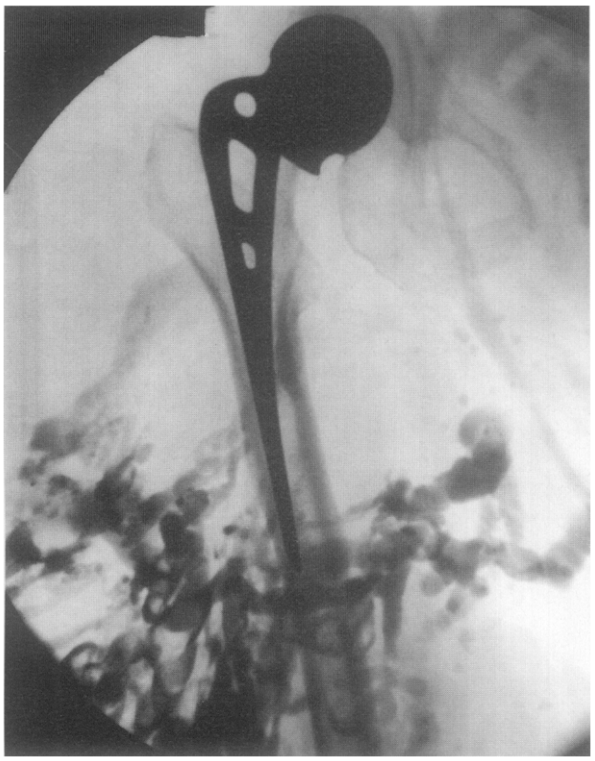

Fig. 2. Venogram demonstrates a large VM from a patient with Klippel-Trenaunay syndrome who experienced continued hemorrhage from her incision site after the placement of a hip prosthesis.

anol injection. Patient 11 was a lady who had a right hip prosthesis placed at an outside institution and experienced continued hemorrhage from her right hip incision. She was reexplored twice, and a hematoma was evacuated and multiple veins were ligated at each operation. She continued to bleed from her incision and was transferred for further care. She was diagnosed as having Klippel-Trenaunay syndrome involving the right leg. Her leg demonstrated the characteristic limb enlargement of this syndrome, and her venogram (Fig. 2) revealed a large VM with absence of the deep venous system. An MRI showed a huge VM extending from the right pelvis to the distal leg with no evidence of arterial communication. Using a combination of ultrasound and direct injection of contrast material, eight varicosities were localized and sclerosed with ethanol injection. Blood continued to ooze from the wound, and the patient was again treated 2 days later. This time seven varicosities were sclerosed, and her bleeding stopped. She had no further trouble with hemorrhage from her wound but was readmitted approximately 5 months later for removal of an infected hip prosthesis, which was probably a result of her two previous

Fig. 3. This T_2 MRI study reveals an extensive, superficial VM of the right thigh. Notice the hyperintense signal (white) of the VM *(closed arrow)* compared with the signal of fat *(open arrow)*.

operative hematoma evacuations rather than the ethanol injections of the superficial varicosities. The patient has had no further problems with hemorrhage and is still able to ambulate with a walker despite the absence of her right hip joint.

Patient 12 had an extensive VM of both legs, right buttocks, penis, and scrotum. He initially complained of spontaneous hemorrhage from his right medial thigh but has also had difficulty with walking and pain. A venogram revealed large, multiple VMs with a normal deep venous system. An MRI showed extensive, superficial VM with no muscular involvement (Fig. 3). Direct injection of ethanol was used to sclerose the bleeding focus, and the patient has had no recurrent bleeding from this area. In addition, he has had trouble walking and wearing shoes related to VM of his feet. Fig. 4 demonstrates direct contrast injection into the lesion before (Fig. 4, *A*) and after *(B)* ethanol sclerosis. To date, this patient has undergone a total of 12 treatments to palliate symptomatic areas, including his feet, ankles, buttock, scrotum, and penis.

DISCUSSION

Direct injection of ethanol into VMs is an effective treatment for focal lesions and can provide palliation of symptomatic areas in extensive lesions. VMs of the head and neck have been treated by this technique and reported in two different series with equally good results. One out of five patients experienced extensive tissue necrosis after extravasation of the ethanol and required application of a split-thickness skin graft in a report by Berthelsen et al.[11] In a

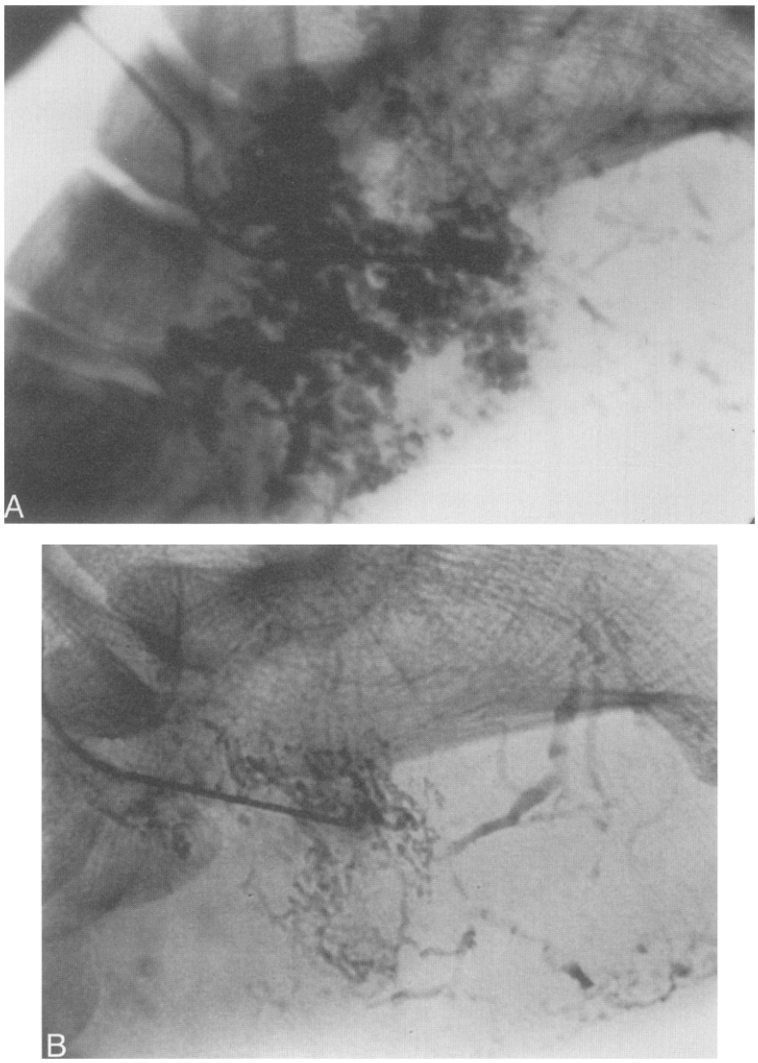

Fig. 4. Extensive VM of the legs that extended onto the right foot is shown with direct injection of contrast material **(A)** and after two injections of ethanol **(B).** Notice the greatly decreased size of the VM after the procedure.

series reported by Svendsen et al.,[1] four of 44 patients (9%) had tissue necrosis that required reconstructive surgery, and a severe paresis of the facial nerve, which resolved spontaneously after 9 months, developed in one patient. The patients' blood alcohol levels were measured in this series before and after ethanol injection, and only three patients (7%) had elevated levels, suggesting that the ethanol was contained in a very localized area. Although extensive tissue necrosis and nerve damage are potential complications with this technique, the present series did not experience any of these major complications, and no extensive operative therapy was needed to control wound complications. Blister formation and skin breakdown was a very common occurrence with this technique but was easily managed with local debridement and wound care in this series.

Various sclerosing agents have been used other than absolute ethanol. Riche et al.[10] have used direct injection of Ethibloc (Ethnor Laboratories, Paris), which is a mixture of ethanol, prolamine, amidotrizoic acid, and oleum papaveris. After injection, the Ethibloc hardens and a mild inflammatory reaction ensues. Patients were taken to the operating room 10 to 12 days after injection, and the lesions were relatively well delineated and excised with minimal blood loss. Six of Riche's patients did not undergo postinjection excision for various reasons. In these patients the swelling of the VM improved within 3 weeks of the injection, and the lesion continued to contract

over the ensuing 2 months. Using absolute ethanol, we have not experienced any need for operative excision in technically successful procedures. Ethibloc is also very viscous, making it more difficult to inject than absolute ethanol.

We have chosen to use absolute ethanol in our institution because of its ability to produce vessel wall necrosis[11,12] and believe that it is the most effective agent currently available, although there are no randomized studies that have compared the various sclerosing agents. Ethanol is used in many different medical applications[1-9,11,12] such as ablation of renal and hepatic tumors, and the use of ethanol in the treatment of VM is well documented in the literature.[1-5,11]

All the patients in this series underwent pretreatment MRI, and several also were followed-up with postprocedure MRI. The VMs all had a characteristic appearance on MRI as previously described,[13,14] with a decreased signal intensity on the T_1-weighted image as compared with fat and a hyperintense signal intensity on the T_2-weighted image. Pathologically, these findings have been correlated with the fibrofatty septa between endothelium-lined vascular channels. MRI can distinguish low-flow VMs from high-flow arteriovenous malformations and fistulas, making arteriograms and venograms unnecessary for the evaluation of most VMs. Early in this series, both arteriograms and venograms were routinely obtained, but currently most patients are initially imaged with MRI only, which is augmented by direct injection of contrast material into the lesion at the time of ethanol sclerosis. Another advantage of MRI is the delineation of vascular, neurologic, and muscular structures that are adjacent or involved with the VM. Other studies, namely venography and arteriography (Fig. 1), do not always show the extent or muscular involvement of the VM.

General anesthesia was used for these procedures because injection with ethanol is very painful. Manipulation of the VM so that the injected ethanol does not extravasate or enter normal venous channels can be time-consuming and is more easily accomplished under general anesthesia. It is also important that the patient does not move the treatment area during the injection of the ethanol. Discomfort after the procedure was controlled using nonsteroidal pain medications, and patients typically reported that the pain lasted 2 to 3 weeks.

CONCLUSION

Ethanol sclerosis is well tolerated, without systemic side effects, and is an effective adjunct to the management of VM. Advantages of ethanol injection include the ability to treat a very localized area without excision as well as the effective treatment of VM that recurred after operative removal. Conversely, extensive lesions may be palliated as symptoms occur. We have found MRI to be the best imaging method for the diagnosis and follow-up of these lesions.

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